

IN THE SPECIFICATION:

Please amend the paragraph at page 5, lines 20-21 as follows:

Figure ~~1~~ shows 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H and 1I show the genomic sequence of SEQ ID NO:5, wherein exons and introns are designated in the genomic sequence of the novel human patched 2 gene.

Please amend the paragraph starting at page 5, line 28 and ending at page 6, line 3 as follows:

A "label" is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include <sup>32</sup>P, fluorescent dyes, electron-dense reagents, enzymes (e.g., as ~~semmonly~~ commonly used in a ELISA), biotin, dioxigenin, or haptens and proteins for which antisera or monoclonal antibodies are available (e.g., the peptide of SEQ ID NO:1 can be made detectable, e.g., by incorporating a radio-label into the peptide, and used to detect antibodies specifically reactive with the peptide).

Please amend the paragraph starting at page 7, line 26 and ending at page 8, line 3 as follows:

The term "target nucleic acid" refers to a nucleic acid (often derived from a biological sample), to which a ~~nucelie~~ nucleic acid probe is designed to specifically hybridise. It is either the presence or absence of the target nucleic acid that is to be detected, or the amount of the target nucleic acid that is to be quantified. The target nucleic acid has a sequence that is complementary to the nucleic acid sequence of the corresponding probe directed to the target. The term target nucleic acid may refer to the specific subsequence of a larger nucleic acid to which the probe is directed or to the ~~ovarall~~ overall sequence (e.g., gene or mRNA) whose expression level it is desired to detect. The difference in usage will be apparent from context.

Please amend the paragraph at page 13, lines 1-26 as follows:

In a specific aspect, the present invention relates to the isolated human genomic PTCH2 nucleic acid comprising parts or all of the genomic sequence denoted SEQ ID NO: 5. In the disclosure of the genomic sequence shown in ~~Fig-1~~ Fig 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H and 1I, the exon/intron structure of the present gene is shown. Further to the exons shown therein, exon 12a and 12b has also been

identified, as specifically defined by SEQ ID NO:3 and SEQ ID NO:4, respectively. Interestingly, there is a splice variant that joins exon 12a to a 3' segment of exon 12b with conservation of the intronic GT-AG dinucleotides. Exons 12a and 12b are not variants, but the actual exons of the gene identified by sequencing the corresponding genomic region. (Materials and methods were as described below ~~described below~~). Accordingly, these findings show that PTCH2 has the same intron/exon structure organization as PTCH1. In another embodiment of this aspect, the present invention relates to a transcript that has skipped only one of the exons 9 and 10 defined in ~~Fig 1~~ Fig 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H and 1I. In an alternative embodiment, the transcript according to the invention has skipped both of exon 9 and 10. The splice variants of the present gene are discussed in more detail below in the section "Results", all of which are included within the scope of the present invention. This aspect of the invention advantageously enables design of suitable PCR primers, which in turn enables screening for mutations of all of the coding sections thereof, e.g. by SSCP analysis, sequencing, or any other suitable method known to someone skilled in this field. Thus, the novel human PTCH2 gene according to the invention has been localized by radiation hybrid mapping to

chromosome 1p32-35 with D1S211 and WI-1404 as closest flanking markers and with an estimated localization 5.5cR from D1S443. This region is often lost by LOH in various different tumor types, such as neuroblastoma, melanoma, breast cancer, colon cancer etc. Accordingly, PTCH2 is a candidate for a tumor suppressor gene in this region and the present invention also encompass diagnostic methods based on this new disclosure.

Please amend the paragraph at page 18, lines 9-17 as follows:

Figure ~~1~~ shows 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H and 1I show the genomic sequence of SEQ ID NO:5, wherein exons and introns are designated in the genomic sequence of the present human patched 2 gene. However, exons 12a and 12b discussed above are not specifically shown in Figure 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H and 1I ~~Figure 1~~, but is instead disclosed as the separate sequences SEQ ID NO:3 and SEQ ID NO:4, respectively. Figure 2A discloses an amino acid sequence comparison of the human PTCH2 (upper lines) and PTCH1 (lower lines) sequences. Vertical lines indicate identical amino acids, while dots similar amino acids. The PTCH2 sequence presented is composed of the original cDNA clones and of the products of the 5' RACE analysis.